1FW A7

Docket No.: 12780/101

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT	:	Leonard et al.
SERIAL NO.	:	09/708,352
FILED	:	November 8, 2000
FOR	:	VACCINES FOR MYCOPLASMA BOVIS AND METHODS OF USE
EXAMINER:		Ford
GROUP ART UNIT	:	1645

Mail Stop: After Final
Commissioner for Patents
P.O. BOX 1450
Alexandria, VA 22313-1450

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop: After Final, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on

Date: March 3, 2008

Signature: Joyce J. Mayer
Genevieve Gil Conaycore

REPLY TO NOTIFICATION OF NON-COMPLIANT APPEAL BRIEF

SIR:

In response to the Notification of Non-compliant Appeal Brief, issued February 5, 2008, the Appellants submit herewith an Amended Appeal Brief.

The Notification of Non-compliant Appeal Brief stated that the original Appeal Brief filed May 22, 2006 failed to comply with 37 C.F.R. §41.37 and 1.116(e) because pages 15-18 of the original Appeal Brief contained new arguments and new evidence, filed after the final Office Action.

In the Amended Appeal Brief enclosed herewith, pages 15-18 of the original Appeal Brief have been removed. In addition, item 5 of the Evidence Appendix, a

reference to *Ex parte Hervy A. Morris*, has been removed. Except for these changes, the Amended Appeal Brief is the same as the original Appeal Brief.

The Appellants believe that the Notification of Non-compliant Appeal Brief was issued in error and are filing concurrently herewith a Petition under 37 C.F.R. §181 to seek withdrawal of the Notification of Non-compliant Appeal Brief.

The Appellants' reasons for filing the Petition are as follows:

(1) Only new evidence, not new arguments, is forbidden by 37 C.F.R. §41.37 and 1.116(e). The original Appeal brief contains no new evidence.

(2) Even if new arguments were forbidden, the original Appeal Brief contains no new arguments.

<u>The original Appeal Brief contains no new evidence</u>

37 C.F.R. §§41.37 and 1.116(e), cited as support for the issuance of the Notification of Non-compliant Appeal Brief, do not mention "new arguments." It would make no sense to rule out a new argument, or a restatement in different terms of a prior argument, in an appeal brief. Otherwise, the appeal brief would serve little function. The Board could simply read the Appellants' prior Office Action response, and there would be little point to asking the Examiner to supply an answer. The arguments in the final rejection would be sufficient.

37 C.F.R. §41.37(c)(2) states:

> (2) A brief shall not include any new or non-admitted amendment, or any new or non-admitted affidavit or other evidence. See § 1.116 of this title for amendments, affidavits or other evidence filed after final action but before or on the same date of filing an appeal and § 41.33 for amendments, affidavits or other evidence filed after the date of filing the appeal.

37 C.F.R. §116(e) states:

> (e) An affidavit or other evidence submitted after a final rejection or other final action (§ 1.113) in an application or in an *ex parte* reexamination filed under § 1.510, or an action closing prosecution (§ 1.949) in an inter partes reexamination filed under § 1.913 but before or on the same date of filing an appeal (§ 41.31 or § 41.61 of this title), may be admitted upon a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented.

37 C.F.R. §41.37(c)(2) refers to "new or non-admitted amendment, or any new or non-admitted affidavit or other evidence" and 37 C.F.R. §116(e) refers to "an affidavit or other evidence submitted after a final rejection or other final action." Pages 15-18 of the original Appeal Brief contain no amendment to the specification or claims, no affidavit, and no new citation of evidence. Thus, 37 C.F.R. §41.37(c)(2) and 37 C.F.R. §116(e) provide no support for the issuance of the Notification of Non-compliant Appeal Brief.

The Notification of Non-compliant Appeal Brief did not specify which item or items on page 15-18 was considered to be new evidence. The evidence appendix of the original Appeal Brief lists 8 items. Items 1-4 and 6-8 are listed together with citations to where those items appeared in the record. Each of items 1-4 and 6-8

appeared in the record before the final rejection was issued. Accordingly, none of items 1-4 and 6-8 can be considered new evidence.

Item 5 is a copy of *Ex parte Hervy A. Morris*, an unpublished decision by the Board of Patent Appeals & Interferences, which was discussed on pages 15-18. Because this decision did not appear in United States Patents Quarterly, a copy of this decision was provided as an exhibit in the Amendment After Final, as a courtesy to the Examiner. That *Ex parte Hervy A. Morris* was provided as an exhibit in order to make it easier for the Examiner to review this decision does not change the fact that *Ex parte Hervy A. Morris* is case law, not new evidence. Thus, the Appellants should not be precluded from relying on *Ex parte Hervy A. Morris* in their Appeal Brief.

Additional considerations arguing for the inclusion of *Ex parte Hervy A. Morris* are that (1) all relevant case law should be made available to the Board of Patent Appeals & Interferences and (2) the Examiner will have an opportunity to address *Ex parte Hervy A. Morris* in the Examiner's Answer.

These considerations argue for the inclusion of *Union Oil Co. of Cal. v. Atlantic Richfield Co.*, 208 F. 3d 989, 54 U.S.P.Q. 2d 1227 (Fed. Cir. 2000) in the Appeal Brief as well.[1] It would be absurd to deny the Appellants the opportunity to rely on, and to deny the Board the benefit of considering, legal authority merely because such authority was not previously cited to the Examiner.

<u>The Appeal Brief does not contain new arguments</u>

---

[1] *Union Oil*, like *Ex parte Hervy A. Morris*, is a case that is discussed on pages 15-18 of the original Appeal Brief.

Pages 15-18 of the original Appeal Brief are directed to an argument that was discussed in an Amendment filed before the Office Action containing a final rejection was issued. That argument is directed to whether certain functional language in the claims ("protective against *Mycoplasma bovis* mastitis") is a real limitation of the claims that serves to distinguish the claims over the prior art. See, e.g., the Amendment filed March 29, 2004, at page 15:

> This recitation makes clear that the functional characteristic of being protective against mastitis is not simply an intended use but rather is a characteristic of the vaccine itself. This characteristic distinguishes over the prior art, such as the vaccine disclosed in Boothby.

The Office Acton containing the final rejection issued May 25, 2005. Thus, this argument was clearly part of the record long before the final rejection and the Appellants were entitled to include it in their Appeal Brief.

Except for the last portion of page 18, all of the discussion on pages 15-18 of the original Appeal Brief is directed to this argument over the meaning of the functional language "protective against *Mycoplasma bovis* mastitis."

Page 15 of the original Appeal Brief begins with a discussion of *Union Oil Co. of Cal. v. Atlantic Richfield Co.*, 208 F. 3d 989, 54 U.S.P.Q. 2d 1227 (Fed. Cir. 2000), in which Appellants argue that *Union Oil* supports their position with respect to the argument over the disputed claim language because *Union Oil* dealt with a similar issue concerning the effect of functional language in claims, albeit in a different field of technology. See page 15, first sentence:

> A much more recent decision, in the Federal Circuit, which specifically dealt with functional characteristics of product claims, and which is therefore particularly applicable to the present application is *Union Oil Co. of Cal. v. Atlantic Richfield Co.*, 208 F. 3d 989, 54 U.S.P.Q. 2d 1227 (Fed. Cir. 2000).

The original Appeal Brief then quoted from portions of *Union Oil* that the Appellants believe support their position on the disputed claim language. The Appellants then went on to state, near the top of page 16: "As in *Union Oil*, claims 29, 30, and 40-44 of the present application recite the functional characteristic at issue – 'protective against *Mycoplasma bovis* mastitis,' " leaving no doubt that this portion of the original Appeal Brief is directed to an argument about the disputed claim language that had already been raised in the Amendment filed March 29, 2004.

The Appellants then used the remaining portion of page 16 to quote portions of the specification that support their arguments with respect to the disputed claim language.

Pages 17 and 18 were directed to a discussion of another case, *Ex parte Hervy A. Morris* (available at 1998 WL 1736155), which was also cited to support Appellants' position on the issue of the disputed claim language concerning protection against mastitis. Following the discussion of *Hervy A. Morris,* at the middle of page 18, the Appellants summed up this portion of the original Appeal Brief by stating: "The evidence of record shows that Boothby I's vaccines were not 'capable of performing the intended use' because the evidence of record shows that Boothby I's vaccines were not protective against mastitis." Again, it is clear that the discussion pertains to the argument over the disputed claim language relating to protection against mastitis.

The material in the last portion of page 18 of the original Appeal Brief appeared on page 16 of the Amendment filed March 29, 2004, before the issuance of the Office Action containing a final rejection on May 25, 2005, and thus does not

contain new arguments. The corresponding portions of page 18 of the original Appeal Brief and page 16 of the Amendment filed March 29, 2004 are as follows:

Original Appeal Brief

Claims 52 and 55

Claims 52 and 55 recite that the vaccine comprises an adjuvant selected from a group that does not include the adjuvants listed in Boothby I.[2] Therefore, Boothby I does not anticipate claims 52 and 55.

---

[2] At page 131, Boothby I discloses the use of the following adjuvants:
Freund's incomplete adjuvant
N-acetylmuramyl-L-alanyl-D-isoglutamine (MDP)
Amphotericin B
Combined magnesium/aluminum hydroxide
Killed *Bordatella pertussis*

Amendment filed March 29, 2004

New independent claim 52 recites that the vaccine comprises an adjuvant that differs from the adjuvants listed in Boothby.[4] Therefore, Boothby does not anticipate new claim 52. New claim 55 depends from new claim 52 and therefore Boothby does not anticipate new claim 55 either.

[4] At page 131, Boothby discloses the use of the following adjuvants:
Freund's incomplete adjuvant
N-acetylmuramyl-L-alanyl-D-isoglutamine (MDP)
Amphotericin B
Combined magnesium/aluminum hydroxide
Killed *Bordatella pertussis*

In view of the above, it is clear that pages 15-18 of the original Appeal Brief do not include new arguments.

That the argument discussed at pages 15-18 of the original Appeal Brief was also discussed in the Amendment After Final does not change the fact that this argument had been raised by the Appellants long before the final rejection issued and thus is not a new argument. It defies common sense to hold that reiterating in an

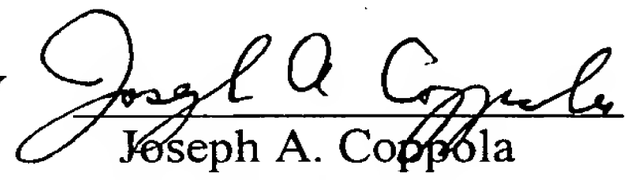
Amendment After Final an argument previously made before the final rejection somehow serves to convert that argument from an old argument to a new argument.

The Notification of Non-compliant Appeal Brief set a date for reply of March 5, 2008. Therefore, it is believed that this response is timely. If this is in error, please treat this response as containing a Petition for the Extension of Time under 37 C.F.R. § 1.136(a) for a period sufficient to permit the filing of this response and charge any corresponding fees to Kenyon & Kenyon's Deposit Account No. 11-0600.

The Appellants hereby make a Conditional Petition for any relief available to correct any defect seen in connection with this paper, or any defect seen to be remaining in this application after this paper. The Commissioner is authorized to charge Kenyon & Kenyon's Deposit Account No. 11-0600 for the Petition fee and any other fees required to effect this Conditional Petition.

Respectfully submitted,

Date: March 3, 2008

BY 
Joseph A. Coppola
Reg. No. 38,413

KENYON & KENYON
One Broadway
New York, NY 10004
(212) 425-7200 (telephone)
(212) 425-5288 (facsimile

OIPE IAP86 MAR 07 2008 PATENT & TRADEMARK OFFICE

12780/101

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS	:	Leonard et al.
SERIAL NO.	:	09/708,352
FILING DATE	:	November 8, 2000
FOR	:	VACCINES FOR MYCOPLASMA BOVIS AND METHODS OF USE
EXAMINER	:	Ford
GROUP ART UNIT	:	1645

Mail Stop: Appeal Brief - Patents
COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, VA 22313-1450

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Appeal Brief - Patents, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on
Date: March 3, 2008
Signature: [signature]

AMENDED APPEAL BRIEF

Table of Contents

Real Party in Interest

The real party in interest for U.S. Patent Application Serial No. 09/708,352 is:

BIOMUNE COMPANY
8906 Rosehill Road
Lenexa, Kansas 66215

Biomune Company is a wholly-owned subsidiary of:

CEVA SANTE ANIMALE S.A.
96, rue de la Victoire, 75009 Paris
FRANCE

Related Appeals and Interferences

There are no related appeals or interferences.

Status of Claims

Claims 1, 3-12, and 29-56 are pending. Claims 1, 3-12, and 29-56 are under rejection and are being appealed. Claims 2, and 13-28 have been canceled.

Status of Amendments

An Amendment under 37 C.F.R. §1.116 (an Amendment after Final) was filed October 24, 2005, 2005 but was not entered.

Summary of Claimed Subject Matter

The invention defined by independent **claim 1** is a vaccine which is protective against *Mycoplasma bovis* clinical disease in a bovine species **{specification, page 4, lines 7-8}** comprising at least one inactivated or attenuated *Mycoplasma bovis* biotype **{specification, page 4, lines 8-9}**, an adjuvant **{specification, page 8, lines 7-8}**, and a pharmaceutically acceptable excipient **{specification, page 4, lines 9-10}**, and wherein the adjuvant does not include saponin **{specification, page 8, lines 7-26, particularly line 21}** and the clinical disease includes respiratory pneumonia **{specification, at Example 7, page 21, line 27 to page 22, line 22, and the abstract}**.

The invention defined by independent **claim 5** is a vaccine which is protective against *Mycoplasma bovis* clinical disease in a bovine species **{specification, page 4, lines 7-8}** comprising at least one inactivated or attenuated *Mycoplasma bovis* biotype **{specification, page 4, lines 8-9}**, an adjuvant **{specification, page 8, lines 7-8}**, and a pharmaceutically acceptable excipient **{specification, page 4, lines 9-10}**, wherein at least one of the inactivated or attenuated *Mycoplasma bovis* biotypes is selected from the group consisting of biotype A **{specification, page 6, line 20}**, biotype B **{specification, page 6, line 20}** and biotype C **{specification, page 6, line 20}**, and wherein the adjuvant does not include saponin **{specification, page 8, lines 7-26, particularly line 21}**.

The invention defined by independent **claim 8** is a vaccine which is protective against *Mycoplasma bovis* clinical disease in a bovine species **{specification, page 4, lines**

7-8} comprising at least two inactivated or attenuated *Mycoplasma bovis* biotypes **{specification, page 9, lines 1-2}** and a pharmaceutically acceptable excipient **{specification, page 4, lines 9-10}**.

The invention defined by independent **claim 29** is a vaccine which is protective against *Mycoplasma bovis* mastitis in a bovine species **{specification, at Example 5, pages 18-20, particularly page 19, lines 17-32, abstract}** comprising at least one inactivated or attenuated Mycoplasma *bovis* biotype **{specification, page page 4, lines 8-9}** and a pharmaceutically acceptable excipient **{specification, page 4, lines 9-10}**.

The invention defined by independent **claim 52** is a whole-cell vaccine **{specification, page 16, lines 22-28}** which is protective against *Mycoplasma bovis* clinical disease in a bovine species **{specification, page 4, lines 7-8}** comprising at least one inactivated or attenuated *Mycoplasma bovis* biotype **{specification, page 4, lines 8-9}** and an adjuvant selected from the group consisting of: an aluminum hydroxide-oil emulsion; a mineral, vegetable, or fish oil-water emulsion; a water-oil-water emulsion; *E. coli* J5; dextran sulfate; iron oxide; sodium alginate; Bacto-Adjuvant; a synthetic polymer; Carbopol; a poly-amino acid; a co-polymer of amino acids; carrageenan; REGRESSIN®; N, N-dioctadecyl-N'-N'-bis(2-hydroxyethyl) propanediamine; a long chain polydispersed β(1,4) linked mannan polymer interspersed with O-acetylated groups; deproteinized cell wall extracts from a non-pathogenic strain of *Mycobacterium*; mannite monooleate; and paraffin oil **{specification, page 8, lines 16-26 and page 11, lines 3-4}**.

The invention defined by independent **claim 56** is a vaccine which is protective against *Mycoplasma bovis* clinical disease in a bovine species **{specification, page 4, lines 7-8}** comprising at least one attenuated *Mycoplasma bovis* biotype **{specification, page 4, lines 8-9}** and a pharmaceutically acceptable excipient **{specification, page 4, lines 9-10}**, wherein the clinical disease includes respiratory pneumonia **{specification, at Example 7, page 21, line 27 to page 22, line 22, and the abstract}**.

Grounds of Rejection to be Reviewed on Appeal

The following grounds of rejection are present in this appeal:

(1) claims 1, 3, 5, 6, 29, 30, 40-44, and 52-55 have been rejected as anticipated under 35 U.S.C. §102(b) by Boothby, Immunologic Responses to Mycoplasma bovis, University Microfilm International (Dissertation) 1-172, 1982 (Boothby I);

(2) claims 1, 4, 5, 7, 29, 30, and 56 have been rejected as anticipated under 35 U.S.C. §102(b) by Thorns et al., 1980, Res. Vet. Sci. 29:328-332 (Thorns); and

(3) claims 1, 3-12, and 29-56 have been rejected as obvious under 35 U.S.C. §103(a) over Boothby I in view of Poumarat et al., 1994, Vet. Microbiol. 40:305-321 (Poumarat) and Thorns.

Argument

Ground of rejection 1

Are claims 1, 3, 5, 6, 29, 30, 40-44, and 52-55 anticipated under 35 U.S.C. §102(b) by Boothby, Immunologic Responses to Mycoplasma bovis, University Microfilm International (Dissertation) 1-172, 1982 (Boothby I)?

Claims 1, 3, 5, 6, 29, 30, 40-44, and 52-55 are rejected as being anticipated by Boothby I. These claims do not stand or fall together, but instead should be grouped according to the subheadings below.

Claims 1, 3, 5, 6, 29, 30, 40-44, and 52-55 (all the claims subject to this rejection)

Boothby's vaccine does not anticipate claims 1, 3, 5, 6, 29, 30, 40-44, and 52-55 because there is a clear difference between the Appellants' vaccine and Boothby I's vaccine. Boothby I's vaccine produces a very unfavorable reaction - all of Boothby I's animals showed hypersensitivity (see Boothby I, page 136, 3rd paragraph: "All groups receiving adjuvant preparations developed delayed-type hypersensitivity …").

In contrast, the presently claimed vaccines do not cause unfavorable reactions. See the specification at page 23, lines 2-3: "No unfavorable reactions resulting from the vaccine's use have been reported;" page 23, lines 14-15: "No unfavorable reactions in animals receiving the product have been reported;" page 20, line 1: "No injection reactions were observed;" and the abstract: "These vaccines demonstrate no undesirable side effects …"

This is a real difference between the Appellants' vaccine and Boothby I that must be due to the nature of the vaccine, and thus indicates that the vaccine of Boothby I does not anticipate the presently claimed vaccine.

Claims 5, 6, and 54

Claim 5 and dependent claims 6 and 54 require that the vaccine comprises particular biotypes that are not disclosed in Boothby I. Claims 5, 6, and 54 each require at least one biotype selected from the group consisting of biotype A, biotype B and biotype C. Boothby I does not disclose biotype A, B, or C. Thus, Boothby I cannot anticipate these claims.

Claims 29, 30, and 40-44

Claims 29, 30, and 40-44 all contain the limitation that the claimed vaccine must be "protective against *Mycoplasma bovis* mastitis in a bovine species." The Examiner argued that this limitation is merely an "intended use" and therefore is not sufficient to avoid anticipation by Boothby I. See the Office Action, dated May 25, 2005, page 4, line 17 to page 5, line 12.

The Appellants do not agree. Being protective against mastitis is not simply an intended use but rather is a functional characteristic of the vaccine itself. The characteristic of being protective against mastitis distinguishes the claims over the prior art, such as the vaccine disclosed in Boothby I. The evidence of record demonstrates that prior art vaccines, such as Boothby I's, were not protective against mastitis. Persons skilled in the art, having knowledge of Boothby I and other prior art, did not view the then-existing vaccines as being protective against mastitis.

For example, Heller et al., 1993, Vet. Microbiol. 37:127-133 (Heller), when referring to methods of controlling the spread of *Mycoplasma bovis*-caused mastitis, did not mention that one should vaccinate to control mastitis but instead stated that culling is necessary. See page 127: "To control the spread of this disease, an early detection of

the pathogen is crucial since the removal and culling of infected cows is necessary to prevent fresh infections."

Hanson, (September, 2001) Bovine Veterinarian 4-8 (Hanson I) and Hanson, (October, 2001) Bovine Veterinarian 12-20 (Hanson II), described methods to prevent mastitis or mitigate its effects, but the methods do not include vaccination, indicating that no vaccine protective against mastitis was known to the art. This failure to mention vaccination is telling, since there clearly was recognition in the art that *Mycoplasma bovis*-caused mastitis was a serious problem. For example, Hanson I, at page 4, quotes a veterinarian as follows:

> "*Mycoplasma* mastitis is a doubly insulting disease," says Blackmer. "Not only can it be remarkably contagious when it is present but it absolutely does not respond to antibiotic therapy. In fact, treatment can actually cause epidemics, because it frequently is spread by unsound intramammary therapy practices."

If vaccination had been available to combat a problem as serious as *M. bovis*-caused mastitis, Heller, Hanson I, and Hanson II would have been expected to mention it, but they did not.

The Office Action dated May 25, 2005, page 5, lines 5-7, refused to consider this evidence, stating: "Applicant's referral to other publications (Heller et al, 1993, Hanson, September 2001 and Hanson, October 2001) to support their position is irrelevant since Boothby teach the claimed vaccine compositions." [emphasis added] However, this misunderstands the import of the evidence. Heller and the two Hanson publications demonstrate that Boothby I does not teach the claimed vaccines. The Appellants submit that the Office Action has assumed the issue to be decided - whether Boothby I discloses the claimed vaccines - before considering all the evidence that should be used to decide that issue. The U.S. Patent & Trademark Office has the burden of proving a case of anticipation, based upon reasoned arguments, after considering all relevant evidence. The Appellants submit that this has not been done.

The Office Action did not explain why, if Boothby I provided a vaccine against mastitis, the art was still recommending culling and other non-vaccine approaches as the only methods of combating mastitis nearly twenty years after Boothby I's disclosure became public.[1] Based on the record as it currently stands, the inevitable conclusion is that Boothby I's vaccine was not protective against mastitis, and thus could not have been the same as the claimed vaccine.

The Office Action dated May 25, 2005 cited *In re Casey*, 370 F. 2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F. 2d 937, 136 USPQ 458 (CCPA 1963) in support of its position with respect to the limitation of protection against mastitis.

Casey is not applicable to the present fact pattern because the functional properties of the claimed device in *Casey* were found to be inherently disclosed in the Kienzle prior art reference. See 370 F. 2d at 941, 152 U.S.P.Q. at 238, where the Court of Customs and Patent Appeals agreed with the reasoning of the Board of Appeals and stated: "The rationale of the board clearly deducible from the language employed is that the Kienzle apparatus as it obviously must be constructed would inherently perform all of the functions called for in claim 1 ..." In the present application, the functional property of being protective against mastitis is not found in the prior art, either explicitly or inherently.

In *Otto*, the claims were rejected for obviousness over a large number of references that collectively disclosed all the limitations recited in the claims. That is not the case here, where the record contains no prior art, either alone or in combination, disclosing the limitation of "protective against bovine mastitis." Instead, the record contains compelling evidence that the prior art lacked this limitation.

---

[1] Boothby I is dated 1982. Heller is dated 1993. Hanson I and Hanson II are dated 2001.

Ground of rejection 2

Are claims 1, 4, 5, 7, 29, 30, and 56 anticipated under 35 U.S.C. §102(b) by Thorns et al., 1980, Res. Vet. Sci. 29:328-332 (Thorns)?

Claims 1, 4, 5, 7, 29, 30, and 56 are rejected as being anticipated by Thorns. These claims do not stand or fall together, but instead should be grouped according to the subheadings below.

Claims 1, 4, 5, 7, 29, 30, and 56 (all of the claims subject to this rejection)

There is a clear difference between the presently claimed vaccines and Thorn's mycoplasma strains. The presently claimed vaccines do not cause unfavorable reactions. See the specification at page 23, lines 2-3: "No unfavorable reactions resulting from the vaccine's use have been reported;" page 23, lines 14-15: "No unfavorable reactions in animals receiving the product have been reported;" page 20, line 1: "No injection reactions were observed;" and the abstract: "These vaccines demonstrate no undesirable side effects …"

All of the strains in Thorns caused some kind of histopathological change. See the right column in Table 1 on page 329, which shows that only the control (i.e., no *Mycoplasma bovis*) injections resulted in no histopathological changes.

Claims 1, 4, 5, 7, 29, 30, and 56 all recite "vaccines" that are "protective" against diseases caused by *Mycoplasma bovis* in bovines. Thorns does not even disclose a vaccine. Thorns discloses only attenuated strains of *Mycoplasma bovis* that were injected into mice. There is no disclosure in Thorns that the attenuated strains were protective against any disease in the injected mice, and certainly not against any disease

in bovines. Thorns does not even disclose any data that indicate the attenuated strains caused any stimulation of the immune systems of the mice against *Mycoplasma bovis.*

Thorns showed that highly passaged strains were attenuated in the sense that the highly passaged strains themselves did not cause responses such as inflammation or abnormal glands to the same degree as low passaged strains. Thus, Thorns disclosed attenuated *Mycoplasma bovis* strains. But claims 1, 4, 5, 7, 29, 30, and 56 are not directed simply to attenuated strains. They are directed to attenuated strains that are capable of functioning as vaccines. Thorns contains no evidence that the attenuated strains disclosed therein could function as vaccines, to protect against disease caused by later exposure to *Mycoplasma bovis*. In particular, Thorns provided no evidence that the mice that were given the attenuated strains were protected from disease when later challenged with *Mycoplasma bovis*. Apparently, Thorns did not even challenge the mice.

The Office Action concluded that, since Thorns's highly attenuated strains did not cause disease themselves, they must have been able to protect against disease, i.e., that the attenuated strains were vaccines. See the Office Action dated May 25, 2005, page 6, lines 2-6:

> Thorns et al teach that all mice that were inoculated with *M. bovis* passaged over 91 times had normal glands and showed not signs of systematic response (page 329, Table 1). Therefore, the mice vaccinated with *M. bovis* passaged over 91 times appeared to be protected against systematic response.

But this logic is fundamentally flawed. It confuses one characteristic - the lack of ability to cause disease - with another, not necessarily related, characteristic - the ability to protect against disease. The Office Action provided no evidence that an attenuated

strain having the former characteristic would necessarily have the second characteristic as well.

Moreover, the authors of Thorns stated that their strains were not vaccines. The authors considered that the work they disclosed only provided information and a starting point for research that might someday "perhaps" lead to the production of a vaccine against *Mycoplasma bovis*. In view of this statement, the strains described in Thorns could not already be vaccines. See page 332, right column, 3rd paragraph:

> Whatever mechanisms the virulent strains have lost or modified, they should provide further insight into the pathogenesis of *M. bovis* mastitis which could perhaps lead to a stable vaccine for this disease. [emphasis added]

Claims 1, 4, 5, and 7

Claims 1, 4, 5, and 7 recite "an adjuvant." Thorns does not disclose an adjuvant. For this reason, Thorns does not anticipate claims 1, 4, 5, and 7.

Claims 29, 30, and 56

Claims 29, 30, and 56 recite the limitations that the claimed vaccines must be "protective against *Mycoplasma bovis* mastitis" (claims 29 and 30) or "protective against *Mycoplasma bovis* clinical disease ... wherein the clinical disease includes respiratory pneumonia" (claim 56). As discussed above in connection with the rejection over Boothby I, these recitations are not simply an "intended use" but instead are functional limitations that confer patentable distinction on the claims. Thorns contains no showing that the attenuated strains disclosed therein are capable of protecting against any diseases. Thus, for this reason as well, Thorns does not anticipate claims 29, 30, and 56.

Ground of rejection 3

Are claims 1, 3-12, and 29-56 obvious over Boothby I in view of Poumarat et al., 1994, Vet. Microbiol. 40:305-321 (Poumarat) and Thorns?

Claims 1, 3-12, and 29-56 have been rejected as being obvious over Boothby I in view of Poumarat et al., 1994, Vet. Microbiol. 40:305-321 (Poumarat) and Thorns. These claims do not stand or fall together, but instead should be grouped according to the subheadings below.

Claims 1, 3-12, and 29-56 (all of the claims subject to this rejection)

As discussed above, the presently claimed vaccine does not cause unfavorable reactions. As discussed above, this limitation is lacking in Boothby I and Thorns, since the *M. bovis* in Boothby I caused hypersensitivity and the *M. bovis* in Thorns caused histopathological changes. Thus, these two publications lack a disclosure of this claim limitation.

As explained more fully below, Poumarat did not disclose vaccines of any kind, and thus failed to teach or suggest a vaccine that does not cause unfavorable reactions.

In view of the complete lack of disclosure of this limitation in the prior art, no combination of the cited references can possibly disclose or suggest this limitation, and the Appellants thus submit that a *prima facie* case of obviousness for claims 1, 3-12, and 29-56 has not been and cannot be made.

Claims 8-12, 31-39, and 46-51

Claims 8-12, 31-39, and 46-51 recite "at least two" *M. bovis* biotypes.

Boothby I does not disclose a vaccine that contains more than one biotype. Even if Thorns is viewed as disclosing vaccines (which the Appellants dispute), Thorns still does not disclose a vaccine containing more than one biotype since all the strains in Thorns were administered individually.

Poumarat does not disclose any vaccines since Poumarat is limited to a study of the antigenic characteristics of certain strains of *Mycoplasma bovis*. Moreover, Poumarat discourages, and thus teaches away from, the use of more than one biotype.

Poumarat divided *Mycoplasma bovis* isolates into 13 different "genomic groups." Poumarat then looked at the antigenic variability between and among these genomic groups. Although Poumarat found much antigenic variability, this variability did not correlate with membership in any particular genomic group. In other words, the same amount of antigenic variability could be found within groups as between groups. See page 318, 2nd paragraph:

> Antigenic profiles of the *M. bovis* strains obtained by immunoblotting with J008 calf serum differed markedly one from the other, the heterogeneity being equally great among strains belonging to the same genomic group and those coming from different genomic groups. There appeared to be no relation between the genomic variability of *M. bovis* and the antigenic variability ...

Because Poumarat teaches that antigenic variability is as great within *Mycoplasma bovis* groups as across *Mycoplasma bovis* groups, Poumarat teaches that there would be no gain in antigenic variability from including more than one type of *Mycoplasma bovis* in a vaccine. That is, there would be no point in having more than one type of *Mycoplasma bovis* in a vaccine. Poumarat thus discourages one of ordinary skill in the art from including more than one biotype in a vaccine, and thus teaches away from the invention defined by claims 8-12, 31-39, and 46-51.

"A prior art reference may be considered to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." *Monarch Knitting Mach. Corp. v. Sulzer Morat GmbH*, 139 F.3d 877, 885, 45 USPQ2d 1977, 1984 (Fed. Cir. 1998).

Claims 34-39 and 46-51

Poumarat's teaching away from a vaccine containing more than one biotype is especially pertinent in connection with claims 34-39 and 46-51. These claims all require that the at least two biotypes be genetically different, as judged by analysis of DNA or RNA. Poumarat expressly teaches that such genetic differences are irrelevant with respect to antigenicity since Poumarat teaches that there appears to be "no relation between the genomic variability of *M. bovis* and the antigenic variability." One of ordinary skill in the art would clearly interpret this conclusion as a teaching that nothing is to be gained from including biotypes that are genetically different in a vaccine, and thus would be discouraged from the invention of claims 34-39 and 46-51. Such a distinct teaching away from the Appellants' invention in the prior art constitutes a strong indication of non-obviousness, and *a fortiori* negates any possible case of *prima facie* obviousness.

Claims 29, 30, and 40-45

Claims 29, 30, and 40-45 recite that the vaccine is "protective against *Mycoplasma bovis* mastitis."

None of Boothby I, Thorns, or Poumarat disclose or suggest this limitation.

Furthermore, there was a long-felt need in the art for an effective vaccine against bovine mastitis. See, e.g., Hanson, (September, 2001) Bovine Veterinarian 4-8 (Hanson I) and Hanson, (October, 2001) Bovine Veterinarian 12-20 (Hanson II), which contain extensive descriptions of the problems caused by bovine mastitis and the difficulty of dealing with this disease. For example, Hanson I quotes a veterinarian as follows (page 4):

> "*Mycoplasma* mastitis is a doubly insulting disease," says Blackmer. "Not only can it be remarkably contagious when it is present but it absolutely does not respond to antibiotic therapy. In fact, treatment can actually cause epidemics, because it frequently is spread by unsound intramammary therapy practices."

The art also discloses that others tried and failed to produce a vaccine protective against mastitis. Boothby et al., 1986, Can. J. Vet. Res. 50:200-204 (Boothby II) shows this failure of others, and also teaches away from the present claims. Boothby II tested whether killed *M. bovis* would be effective as a vaccine against bovine mastitis and found that it was not. Despite their prior exposure to killed *M. bovis*, the treated cows in Boothby II were not protected against infection (see page 202, middle column: "All experimentally challenged quarters became infected ..."). Thus, Boothby II was unsuccessful. Such a failure is a clear and strong deterrent to others. The skilled person therefore would undoubtedly have been deterred and discouraged by Boothby II from attempting to produce *M. bovis* vaccine, and thus would not even have sought the solution provided by the Appellants.

Moreover, the treated animals in Boothby II showed poorer milk production than the untreated animals. The treated cows suffered significant and persistent reductions in the level of milk production. The control cows exhibited a smaller and more transient drop in milk production. See Figure 2 on page 202 for a comparison of treated and control cows. Thus, not only did the killed *M. bovis* fail to protect the treated cows, but

it caused milk production to be even worse than it would have been had the cows not been treated. Since the primary purpose for having dairy herds is to produce milk, one of ordinary skill in the art would certainly be deterred by a result that decreased the production of milk.[2] Given that Boothby would have deterred the skilled person in two major respects - lack of efficacy and decrease in milk production - Boothby must be seen as teaching away from the Appellants' invention.

Claim 56

Claim 56 is directed to attenuated vaccines that are protective against respiratory pneumonia.

Boothby I and Poumarat do not disclose attenuated *Mycoplasma bovis*. As discussed above, although Thorns does disclose attenuated strains of *Mycoplasma bovis,* Thorns states that these strains are not vaccines, but might provide "further insight" which could "perhaps" lead to the development of a vaccine. See Thorns, page 332, right column, 3rd paragraph:

> Whatever mechanisms the virulent strains have lost or modified, they should provide further insight into the pathogenesis of *M. bovis* mastitis which could perhaps lead to a stable vaccine for this disease. [emphasis added]

Given the lack of disclosure of an attenuated vaccine that is protective against respiratory pneumonia in any of Boothby I, Thorns, or Poumarat, and the lack of any suggestion as to how such a vaccine could be produced in those references, it cannot properly be said that those references make obvious claim 56.

---

[2] This is recognized by Boothby II at page 200, right column, where it is stated: "If prophylactic vaccination is to be efficacious, it must have minimal effects on the health and productive capabilities of

CONCLUSION

For the reasons discussed above, the Appellants respectfully request that the Board of Patent Appeals and Interferences reverse:

(1) the rejection of claims 1, 3, 5, 6, 29, 30, 40-44, and 52-55 as anticipated under 35 U.S.C. §102(b) by Boothby, Immunologic Responses to Mycoplasma bovis, University Microfilm International (Dissertation) 1-172, 1982 (Boothby I);

(2) the rejection of claims 1, 4, 5, 7, 29, 30, and 56 as anticipated under 35 U.S.C. §102(b) by Thorns et al., 1980, Res. Vet. Sci. 29:328-332 (Thorns); and

(3) the rejection of claims 1, 3-12, and 29-56 as obvious under 35 U.S.C. §103(a) over Boothby I in view of Poumarat et al., 1994, Vet. Microbiol. 40:305-321 (Poumarat) and Thorns.

Respectfully submitted,

Dated: MARCH 3, 2008

Joseph A. Coppola
Reg. No. 38,413
KENYON & KENYON
One Broadway
New York, NY 10004
Tel.: (212) 452-7200
Fax: (212) 452-5288

---

the cow."

CLAIMS APPENDIX

1. A vaccine which is protective against *Mycoplasma bovis* clinical disease in a bovine species comprising at least one inactivated or attenuated *Mycoplasma bovis* biotype, an adjuvant, and a pharmaceutically acceptable excipient, and wherein the adjuvant does not include saponin and the clinical disease includes respiratory pneumonia.

2. canceled

3. The vaccine of claim l, wherein the *Mycoplasma bovis* biotype is inactivated and the amount of each inactivated biotype is at least 10^8 *M.* bovis cells.

4. The vaccine of claim 1, wherein the *Mycoplasma bovis* biotype is attenuated and the amount of each attenuated biotype is at least 10^5 *M. bovis* cells.

5. A vaccine which is protective against *Mycoplasma bovis* clinical disease in a bovine species comprising at least one inactivated or attenuated *Mycoplasma bovis* biotype, an adjuvant, and a pharmaceutically acceptable excipient, wherein at least one of the inactivated or attenuated *Mycoplasma bovis* biotypes is selected from the group consisting of biotype A, biotype B and Biotype C, and wherein the adjuvant does not include saponin.

6. The vaccine of claim 5, wherein the *Mycoplasma bovis* biotype is inactivated and the amount of each selected inactivated *Mycoplasma bovis* biotype is at least 10^8 *M. bovis* cells.

7. The vaccine of claim 5, wherein the *Mycoplasma bovis* biotype is attenuated and the amount of each selected attenuated *Mycoplasma bovis* biotype is at least 10^5 *M. bovis* cells.

8. A vaccine which is protective against *Mycoplasma bovis* clinical disease in a bovine species comprising at least two inactivated or attenuated *Mycoplasma bovis* biotypes and a pharmaceutically acceptable excipient.

9. The vaccine of claim 8, further comprising a suitable adjuvant.

10. The vaccine of claim 8, wherein the *Mycoplasma bovis* biotype is inactivated and the amount of each inactivated biotype is at least 10^8 *M. bovis* cells.

11. The vaccine of claim 8, wherein the *Mycoplasma bovis* biotype is attenuated and the amount of each attenuated biotype is at least 10^5 *M. bovis* cells.

12. The vaccine of claim 8, wherein the *Mycoplasma bovis* biotypes are selected from the group consisting of biotype A, biotype B and biotype C.

13-28. (canceled)

29. A vaccine which is protective against *Mycoplasma bovis* mastitis in a bovine species comprising at least one inactivated or attenuated Mycoplasma *bovis* biotype and a pharmaceutically acceptable excipient.

30. The vaccine of claim 29, where the vaccine is protective against *Mycoplasma bovis* mastitis in a bovine species following systemic administration.

31. The vaccine of claim 30, comprising at least two inactivated *Mycoplasma bovis* biotypes.

32. The vaccine of claim 31, wherein the vaccine includes at least one inactivated *Mycoplasma bovis* biotype selected from the group consisting of biotype A, biotype B and biotype C.

33. The vaccine of claim 31 wherein the vaccine contains approximately 10^8 cells of each biotype in a volume of 2-5 milliliters.

34. The vaccine of claim 8 wherein the at least two inactivated or attenuated *Mycoplasma bovis* biotypes are genetically different as determined by an analysis of DNA or RNA from the biotypes.

35. The vaccine of claim 34 wherein the analysis is by PCR fingerprinting, analysis of ribosomal RNA, or analysis of DNA polymorphisms.

36. The vaccine of claim 35 wherein the analysis is by PCR fingerprinting.

37. The vaccine of claim 36 wherein the PCR fingerprinting uses arbitrarily chosen primers.

38. The vaccine of claim 37 wherein the PCR fingerprinting uses as primers 5' NNN NCG NCG NCA TCN GGC 3' (SEQ ID NO:1) and 5' NCG NCT TAT CNG GCC TAC 3' (SEQ ID NO:2).

39. The vaccine of claim 8 wherein the at least two *Mycoplasma bovis* biotypes have been identified as being different biotypes by a process comprising:
(a) isolating DNA from the biotypes;
(b) amplifying the DNA by PCR;
(c) separating the amplified DNA by gel electrophoresis; and
(d) comparing the resulting patterns from the gel electrophoresis to identify the different biotypes.

40. The vaccine of claim 30 wherein, when the vaccine is administered to a plurality of cows in a herd of cows, the incidence of mastitis caused by *Mycoplasma bovis* in the herd before administering is greater than the incidence of mastitis caused by *Mycoplasma bovis* in the herd after administering.

41. The vaccine of claim 40 wherein the vaccine is administered to at least about 50% of the herd.

42. The vaccine of claim 41 where the vaccine is administered together with an adjuvant.

43. The vaccine of claim 42 wherein the adjuvant is an aluminum hydroxide-oil emulsion; a mineral, vegetable, or fish oil-water emulsion; a water-oil-water emulsion; incomplete Freund's adjuvant; *E. coli* J5; dextran sulfate; iron oxide; sodium alginate; Bacto-Adjuvant; a synthetic polymer; Carbopol; a poly-amino acid; a co-polymer of amino acids; saponin; carrageenan; REGRESSIN®; N, N-dioctadecyl-N'-N'-bis(2-hydroxyethyl) propanediamine; a long chain polydispersed β(1,4) linked mannan polymer interspersed with O-acetylated groups; deproteinized cell wall extracts from a non-pathogenic strain of *Mycobacterium*; mannite monooleate; paraffin oil; or muramyl dipeptide.

44. The vaccine of claim 30 where the *Mycoplasma bovis* biotype is inactivated and has been inactivated by treatment with: formalin, azide, freeze-thawing, sonication, heat, sudden pressure drop, detergent, lysozyme, phenol, proteolytic enzymes, β-propiolactone, Thimerosal, or binary ethyleneimine.

45. The vaccine of claim 44 where the *Mycoplasma bovis* biotype has been inactivated by treatment with β-propiolactone.

46. The vaccine of claim 31 wherein the at least two inactivated *Mycoplasma bovis* biotypes are genetically different as determined by an analysis of DNA or RNA from the biotypes.

47. The vaccine of claim 46 wherein the analysis is by PCR fingerprinting, analysis of ribosomal RNA, or analysis of DNA polymorphisms.

48. The vaccine of claim 47 wherein the analysis is by PCR fingerprinting.

49. The vaccine of claim 48 wherein the PCR fingerprinting uses arbitrarily chosen primers.

50. The vaccine of claim 49 wherein the PCR fingerprinting uses as primers 5' NNN NCG NCG NCA TCN GGC 3' (SEQ ID NO:1) and 5' NCG NCT TAT CNG GCC TAC 3' (SEQ ID NO:2).

51. The vaccine of claim 31 wherein the at least two *Mycoplasma bovis* biotypes have been identified as being different biotypes by a process comprising:
(a) isolating DNA from the biotypes;
(b) amplifying the DNA by PCR;
(c) separating the amplified DNA by gel electrophoresis; and
(d) comparing the resulting patterns from the gel electrophoresis to identify the different biotypes.

52. A whole-cell vaccine which is protective against *Mycoplasma bovis* clinical disease in a bovine species comprising at least one inactivated or attenuated *Mycoplasma bovis* biotype and an adjuvant selected from the group consisting of: an aluminum hydroxide-oil emulsion; a mineral, vegetable, or fish oil-water emulsion; a water-oil-water emulsion; *E. coli* J5; dextran sulfate; iron oxide; sodium alginate; Bacto-Adjuvant; a synthetic polymer; Carbopol; a poly-amino acid; a co-polymer of amino acids; carrageenan; REGRESSIN®; N, N-dioctadecyl-N'-N'-bis(2-hydroxyethyl) propanediamine; a long chain polydispersed β(1,4) linked mannan polymer interspersed with O-acetylated groups; deproteinized cell wall extracts from a non-pathogenic strain of *Mycobacterium*; mannite monooleate; and paraffin oil.

53. The vaccine of claim l, wherein the *Mycoplasma bovis* biotype is inactivated.

54. The vaccine of claim 5, wherein the *Mycoplasma bovis* biotype is inactivated.

55. The vaccine of claim 52, wherein the *Mycoplasma bovis* biotype is inactivated.

56. A vaccine which is protective against *Mycoplasma bovis* clinical disease in a bovine species comprising at least one attenuated *Mycoplasma bovis* biotype and a

pharmaceutically acceptable excipient, wherein the clinical disease includes respiratory pneumonia.

Evidence Appendix

The evidence relied upon, and where in the record that evidence was entered, is as follows:

1. Boothby, Immunologic Responses to Mycoplasma bovis, University Microfilm International (Dissertation) 1-172, 1982 (Boothby I). Boothby I was applied by the Examiner in an anticipation rejection in the Office Action dated May 25, 2005, bottom of page 2 to middle of page 5.
2. Heller et al., 1993, Vet. Microbiol. 37:127-133 (Heller). Heller was submitted in an Information Disclosure Statement filed April 16, 2002. The Examiner returned a copy of the PTO-1449 Form accompanying this Information Disclosure Statement, with the entry for this publication initialed, with the Office Action dated September 30, 2003.
3. Hanson, (September, 2001) Bovine Veterinarian 4-8 (Hanson I). Hanson I was submitted in an Information Disclosure Statement filed April 16, 2002. The Examiner returned a copy of the PTO-1449 Form accompanying this Information Disclosure Statement, with the entry for this publication initialed, with the Office Action dated September 30, 2003.
4. Hanson, (October, 2001) Bovine Veterinarian 12-20 (Hanson II). Hanson II was submitted in an Information Disclosure Statement filed April 16, 2002. The Examiner returned a copy of the PTO-1449 Form accompanying this Information Disclosure Statement, with the entry for this publication initialed, with the Office Action dated September 30, 2003.

5. Thorns et al., 1980, Res. Vet. Sci. 29:328-332 (Thorns). Thorns was applied by the Examiner in an anticipation rejection in the Office Action dated May 25, 2005, middle of page 5 to middle of page 7.

6. Poumarat et al., 1994, Vet. Microbiol. 40:305-321 (Poumarat). Poumarat was applied by the Examiner in an anticipation rejection in the Office Action dated May 25, 2005, middle of page 7 to top of page 12.

7. Boothby et al., 1986, Can. J. Vet. Res. 50:200-204 (Boothby II). Boothby II was submitted in an Information Disclosure Statement filed April 16, 2002. The Examiner returned a copy of the PTO-1449 Form accompanying this Information Disclosure Statement, with the entry for this publication initialed, with the Office Action dated September 30, 2003.

Related Proceedings Appendix

(none)